

### **Complete Listing of Claims Pursuant to 37 C.F.R. §1.121**

Pursuant to 37 C.F.R. §1.121 the following is a complete listing of the claims of the present application. In this set of claims, please amend the claims as follows. The following listing of claims will replace all prior versions of claims in the application:

#### **Listing of the Claims:**

1.-32. (canceled)

33. (previously presented) An antibody that binds phosphorylated tau as set out in SEQ ID NO: 1, wherein the antibody binds a tau epitope comprising a serine or threonine residue only when the serine or threonine residue is phosphorylated, said serine or threonine residue selected from the group consisting of

- (a) residue 46 in SEQ ID NO:1;
- (b) residue 50 in SEQ ID NO:1;
- (c) residue 52 in SEQ ID NO:1;
- (d) residue 68 in SEQ ID NO:1;
- (e) residue 69 in SEQ ID NO:1;
- (f) residue 71 in SEQ ID NO:1;
- (g) residue 111 in SEQ ID NO:1;
- (h) residue 113 in SEQ ID NO:1;
- (i) residue 153 in SEQ ID NO:1;
- (j) residue 175 in SEQ ID NO:1;
- (k) residue 182 in SEQ ID NO:1;
- (l) residue 184 in SEQ ID NO:1;
- (m) residue 198 in SEQ ID NO:1;
- (n) residue 199 in SEQ ID NO:1;

- (o) residue 202 in SEQ ID NO:1;
- (p) residue 205 in SEQ ID NO:1;
- (q) residue 208 in SEQ ID NO:1;
- (r) residue 210 in SEQ ID NO:1;
- (s) residue 212 in SEQ ID NO:1;
- (t) residue 214 in SEQ ID NO:1;
- (u) residue 217 in SEQ ID NO:1;
- (v) residue 220 in SEQ ID NO:1;
- (w) residue 231 in SEQ ID NO:1;
- (x) residue 235 in SEQ ID NO:1;
- (y) residue 237 in SEQ ID NO:1;
- (z) residue 238 in SEQ ID NO:1;
- (aa) residue 262 in SEQ ID NO:1;
- (bb) residue 263 in SEQ ID NO:1;
- (cc) residue 293 in SEQ ID NO:1;
- (dd) residue 324 in SEQ ID NO:1;
- (ee) residue 356 in SEQ ID NO:1;
- (ff) residue 361 in SEQ ID NO:1;
- (gg) residue 400 in SEQ ID NO:1;
- (hh) residue 403 in SEQ ID NO:1;
- (ii) residue 404 in SEQ ID NO:1; and
- (jj) residue 422 in SEQ ID NO:1.

34. (previously presented) The antibody of claim 33, wherein the serine or threonine residue is selected from the group consisting of

- (a) residue 46 in SEQ ID NO:1;

- (b) residue 50 in SEQ ID NO:1;
- (c) residue 69 in SEQ ID NO:1;
- (d) residue 111 in SEQ ID NO:1;
- (e) residue 153 in SEQ ID NO:1;
- (f) residue 175 in SEQ ID NO:1;
- (g) residue 181 in SEQ ID NO:1;
- (h) residue 199 in SEQ ID NO:1;
- (i) residue 202 in SEQ ID NO:1;
- (j) residue 205 in SEQ ID NO:1;
- (k) residue 212 in SEQ ID NO:1;
- (l) residue 217 in SEQ ID NO:1;
- (m) residue 231 in SEQ ID NO:1;
- (n) residue 235 in SEQ ID NO:1;
- (o) residue 262 in SEQ ID NO:1;
- (p) residue 404 in SEQ ID NO:1; and
- (q) residue 422 in SEQ ID NO:1;

35. (previously presented) The antibody of claim 33, wherein the serine residue is residue 262 in SEQ ID NO:1.

36. (previously presented) The antibody of claim 33, wherein the antibody is a  $F_{ab}$  fragment.

37. (previously presented) The antibody of claim 33, wherein the antibody is a monoclonal antibody.

38. (previously presented) A hybridoma that produces an antibody of claim 37.

39. (previously presented) A method of detecting a phosphorylated tau protein as set out in SEQ ID NO: 1 comprising

(a) contacting a sample comprising a tau protein with an antibody that binds phosphorylated tau according to claim 33; and

(b) detecting binding of the antibody to phosphorylated tau protein.

40. (presently amended) The method of claim 39, wherein the antibody ~~phosphorylated residue-binding antibody~~ binds phosphorylated serine residue 262 in SEQ ID NO:1.

41. (withdrawn) An isolated protein kinase that converts tau protein to Alzheimer's tau protein by phosphorylating serine residues in Ile-Gly-Ser or Cys-Gly-Ser motifs of the tau protein, wherein the protein kinase

(a) has a molecular weight of 70 kD;

(b) is unable to bind Q-Sepharose;

(c) is able to bind S-Sepharose;

(d) elutes at 250 mM NaCl during S-Sepharose chromatography;

(e) elutes at 250 mM NaCl during heparin agarose chromatography;

(f) elutes at 150 mM NaCl during Mono Q chromatography;

(g) has an alkaline pI;

(h) incorporates 3 or 4 phosphates into a tau protein selected from the group consisting of htau34, htau40, htau23, and construct K19;

(i) does not phosphorylate a mutant of K19, wherein the mutant contains mutations of serine residues 262, 293, 324, and 356 to alanine residues; and

(j) phosphorylates serine residues 262, 293, 324, and 356 of tau protein.

42. (withdrawn) The isolated kinase of claim of claim 41, wherein the protein kinase is isolated from brain tissue.

43. (withdrawn) An antibody that specifically binds the protein kinase of claim 41.

44. (withdrawn) The antibody of claim 43, wherein the antibody is a monoclonal antibody.

45. (withdrawn) The antibody of claim 43, wherein the antibody binds to the kinase preventing the kinase from converting tau protein to Alzheimer's tau protein by inhibiting phosphorylation of serine residues in Ile-Gly-Ser or Cys-Gly-Ser motifs of the tau protein by the kinase.

46. (withdrawn) A composition comprising the antibody of claim 45 and a pharmaceutically accepted carrier.

47. (withdrawn) A method of identifying a candidate inhibitor of a protein kinase of claim 41, the method comprising the steps of:

(a) contacting a composition comprising the protein kinase with a substrate and a test compound;

(b) measuring kinase activity of the protein kinase; and

(c) comparing kinase activity when the protein kinase is contacted with the test compound to kinase activity when the protein kinase is not contacted with the test compound, wherein a decrease in kinase activity when the protein kinase is contacted with the test compound indicates a candidate inhibitor.

48. (withdrawn) The method of claim 47, wherein the test compound is selected from the group consisting of an antibody, a polypeptide, and an oligopeptide.

49. (withdrawn) The method of claim 47, wherein the substrate is tau protein.

50. (withdrawn) The method of claim 49, wherein kinase activity is measured by determining phosphorylation of the tau protein.

51. (withdrawn) The method of claim 50, wherein phosphorylation of a tau amino acid selected from a group consisting of serine residue 262, 293, 324, and 356 of tau protein is determined.

52. (withdrawn) The method of claim 51, wherein phosphorylation of serine residues 262, 293, 324, and 356 of tau protein is determined.

53. (withdrawn) The method of claim 47, wherein kinase activity is measured by determining tau-microtubule binding.

54. (withdrawn) An isolated protein kinase that converts tau protein to Alzheimer's tau protein by phosphorylating serine residues in Ile-Gly-Ser or Cys-Gly-Ser motifs of the tau protein, wherein the protein kinase

- (a) has a molecular weight of 35 kD;
- (b) is unable to bind to Mono S;
- (c) is able to bind to Mono Q;
- (d) has an acidic pI;
- (e) incorporates a phosphate amount of 3.2 Pi into htau34, 3.4 Pi into htau40, 3.3 Pi into htau23, and 2.8 Pi into mutant htau23 (Ser262 to Ala);
- (f) phosphorylates serine residues 262, 293, 324, and 356 of tau protein.

55. (withdrawn) The isolated kinase of claim of claim 54, wherein the protein kinase is isolated from brain tissue.

56. (withdrawn) An antibody that specifically binds the protein kinase of claim 54.

57. (withdrawn) The antibody of claim 56, wherein the antibody is a monoclonal antibody.

58. (withdrawn) The antibody of claim 56, wherein the antibody binds to the kinase preventing the kinase from converting tau protein to Alzheimer's tau protein by inhibiting phosphorylation of serine residues in Ile-Gly-Ser or Cys-Gly-Ser motifs of the tau protein by the kinase.

59. (withdrawn) A composition comprising the antibody of claim 58 and a pharmaceutically accepted carrier.

60. (withdrawn) A method of identifying a candidate inhibitor of a protein kinase of claim 54, the method comprising the steps of:

(a) contacting a composition comprising the protein kinase with a substrate and a test compound;

(b) measuring kinase activity of the protein kinase; and

(c) comparing kinase activity when the protein kinase is contacted with the test compound to kinase activity when the protein kinase is not contacted with the test compound, wherein a decrease in kinase activity when the protein kinase is contacted with the test compound indicates a candidate inhibitor.

61. (withdrawn) The method of claim 60, wherein the test compound is selected from the group consisting of an antibody, a polypeptide, and an oligopeptide.

62. (withdrawn) The method of claim 60, wherein the substrate is tau protein.

63. (withdrawn) The method of claim 62, wherein kinase activity is measured by determining phosphorylation of the tau protein

64. (withdrawn) The method of claim 63, wherein phosphorylation of a tau amino acid selected from a group consisting of serine residue 262, 293, 324, and 356 of tau protein is determined.

65. (withdrawn) The method of claim 64, wherein phosphorylation of serine residues 262, 293, 324, and 356 of tau protein is determined.

66. (withdrawn) The method of claim 60, wherein kinase activity is measured by determining tau-microtubule binding.